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The Heterogeneity of Pulmonary Hypertension Nomenclature in Empiric Research Studies: Systematic Findings From Three Western European Countries

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ABSTRACT

This systematic literature review of three Western European Countries identified $N = 48$ different terms to describe pulmonary arterial pressure and $N = 35$ thresholds used to define pulmonary hypertension in published empiric research studies. There is an urgent need to standardize pulmonary artery pressure nomenclature and pulmonary hypertension definitions in clinical research reports.

1 | Introduction

The first definition of pulmonary hypertension (PH) was published in 1973 and stipulated that right heart catheterization (RHC) is needed for diagnosis [1]. However, RHC is invasive and generally reserved for patients with moderate to severe PH symptoms. Transthoracic echocardiography, by contrast, is noninvasive and often the first quantitative test used to assess the probability of PH [2], but alone is insufficient to diagnose (or stage) PH in clinical practice. Confusion related to the use of two modalities for assessing PH is compounded further by greater availability of echocardiography [3] compared to RHC especially in resource-limited settings, evolving clinical indications for RHC to assess PH, and heterogeneity in practice patterns for using either test in the management of patients. Ultimately, international consensus guidelines recommend the incorporation of echocardiography and RHC data for staging and prognosticating PH in clinical practice [2, 4].

Although the approach to diagnosing PH is evidence-based, intricacies in assessing patients could affect the framework for including PH patients in empiric research. Since data from clinical, epidemiologic, and population health studies are used to inform virtually all aspects of PH, including prevalence, prognosis, and clinical decision-making, it is important to determine if variable approaches for describing PH persist in the literature. Heterogeneity reporting PH in research is, in turn, consequentially positioned to destandardize the PH definition and introduce bias when describing fundamental information on the clinical profile of patient cohorts. This is particularly important when considering aspects of PH that are important to global health, including the availability of echocardiography and RHC. To understand the scope of this dilemma, we

quantitated heterogeneity in the PH definitions that are used in contemporary research studies.

2 | Methods

We performed a systematic literature search using the PubMed (Medline) database for original publications between 1945 and 2023 without age or language restriction in Austria, Germany, and Switzerland as part of a wider effort to profile the global prevalence of PH. We used three independent, predefined search strings employing MESH terms ("pulmonary hypertension," "echocardiography" or "echocardiogram," and "right heart catheterization" or "pulmonary catheter") for each country. We included all studies in which PH prevalence was (i) directly provided by the authors, (ii) based on pulmonary artery pressure (PAP) recorded from RHC, or (iii) inferred using PAP estimates from echocardiography. For all studies that were assessed by full-text review, we extracted the terms used to describe PAP as well as the definitions used to define PH.

3 | Results

In total, we identified 186 publications between 1985 and 2023 of which $N = 158$ (85.0%) were published between 2013 and 2023. There were $N = 51$ (27.4%) publications in which PH prevalence was provided directly by the authors, whereas $N = 91$ (48.9%) publications reported PH prevalence using systolic pulmonary arterial pressure (sPAP) from echocardiography and $N = 44$ (23.7%) used mean PAP (mPAP) from RHC. We identified $N = 48$ different PAP criteria used to define PH: $N = 36$ for echocardiography and $N = 12$ for RHC. There were also $N = 35$ different definitions provided by authors to diagnose PH (Table 1). Further, only 38% of these studies used criteria that aligned with an international consensus definition of PH (mPAP at rest measured by RHC > 20 mmHg after 2022 or ≥ 25 mmHg before 2022) or measurement that was consistent with the recommended criteria for using echocardiography to establish elevated probability of PH (sPAP > 36 mmHg calculated from tricuspid regurgitation velocity > 2.8 m/s^2. Of note, none of the studies included in our analysis aimed to study "severe" PH only to explain elevated cutoffs that were used to define PH.

4 | Discussion

These data show that a multiplicity of criteria are used to define PH in empiric analyses, highlighting poor adherence to evidence-based recommendations for profiling PH in research reports. The use of inconsistent PAP nomenclature in research is expected to confound accuracy of PH epidemiologic data and promote confusion in the approach and management of patients in clinical practice. Data from this study letter, thus, cast new light on a largely unrecognized need in PH: standardization of nomenclature to improve the fidelity of clinical and population health research studies.

In 2015, the European Society of Cardiology (ESC)/European Respiratory Society (ERS) Guidelines on PH recommended for the first time that tricuspid regurgitation velocity (TRV) assessed by echocardiographic be used as a key test in the assessment of at-risk patients [5]. In doing so, the PH community acknowledged the limitations of ultrasonographic PAP estimates and reinforced the need for hemodynamic data collected invasively to establish a diagnosis, but also recognized that relying solely on RHC when evaluating PH is likely to exclude as sizeable cohort of patients for whom a treatable form of pulmonary vascular disease may ultimately be discoverable. Thus, TRV > 2.8 m/s and TRV > 3.4 m/s emerged as criteria defining a low and high probability of PH by echocardiography, respectively [2]. However, our observations suggest little adherence to these guidelines in clinical research and that arbitrary (and widely variable) TRV (sPAP) thresholds are used to build PH patient cohorts. Uncoupling the framework defining PH under research versus clinical circumstances adds unnecessary heterogeneity to studies that focus on disease prevalence and outcome risks. Adherence to a common nomenclature is particularly important also to understanding longitudinal profiles of PH, which is itself part of a growing priority in real-world datasets to minimize selection and health inequity bias that often affects studies using referral populations.

In the broad perspective of global and regional health policy makers, PH is often viewed as a rare disease that affects only a small number of patients. This is partly because PH is frequently incorrectly interpreted to be synonymous with pulmonary arterial hypertension (PAH), which is a disease that accounts for only ~6% of all PH cases [2]. Notably, PH is itself an independent driver of adverse outcomes in many diseases that are known to affect health burden worldwide, including left heart failure, chronic obstructive pulmonary disease, and human immunodeficiency virus [6, 7]. In these clinical scenarios, the development of PH is common and invariably associated with clinical worsening and increased mortality. Even mildly elevated PAP, both in RHC and echocardiography, is associated with pathogenic changes to right ventricular structure and function and increases the probability of 3-year mortality by around 25% compared to similar patients without PH [8, 9]. The broad use of varying definitions of PH and heterogenous nomenclature to describe PH hinders our ability to summarize current prevalence data systematically. We believe that this is partly because PH is still poorly understood by non-PH experts, which in turn may also lead to problems in translating PH research into clinical practice globally. Indeed, accurately defining PH has implications for all: researchers, physicians, and patients.

It is timely to standardize the nomenclature for PAP and TRV used in clinical research reports in line with the current PH definition suggested by international consensus documents [2, 4]. The peer-review process should prioritize consistency between PH definitions used in research with contemporary definitions set forth by consensus proceedings or request evidence-based explanations to account for variations. Additionally, reporting quantitative data (i.e., numerical means) for PAP and TRV rather than relying on binary categorizations of PH (present vs. absent based relative to a single threshold) is also likely to improve knowledge of the relationship between PH stage with prevalence and outcome. If a study investigating PH severity uses hemodynamic threshold values that deviate from the currently accepted PH definition, both the chosen threshold and the accepted PH threshold from guideline

TABLE 1 | Heterogenous PAP Nomenclature (alphabetical order; left column) and PAP thresholds used to define PH (right column) in the literature based on echocardiographic (ECHO) or right heart catheterization (RHC) procedures.

PAP Nomenclature in ECHO and RHC	PH definitions in the literature
Arterial pulmonary mean pressure	sPAP > 30 mm Hg (Echo)
Delta RV/RA pressure	sPAP > 33 mm Hg (Echo)
Delta RVSP–RAP	sPAP > 34 mm Hg (Echo)
Mean arterial pulmonary pressure	sPAP ≥ 35 mm Hg (Echo)
Mean PA pressure	sPAP > 35 mm Hg (Echo)
Mean PAP	sPAP > 35 mm Hg (Echo) or symptomatic exertional dyspnea without any other known reason
Mean pulmonary arterial pressure	sPAP > 36 mm Hg (Echo)
Mean pulmonary artery pressure	sPAP > 40 mm Hg (Echo)
Mean pulmonary pressure	sPAP > 45 mm Hg (Echo)
PA pressure	sPAP ≥ 50 mm Hg (Echo)
PA systolic pressure	sPAP > 50 mm Hg (Echo)
PAmean	sPAP ≥ 55 mm Hg (Echo)
PAMP (pulmonary arterial mean pressure)	sPAP > 60 mm Hg (Echo)
PAP	sPAP ≥ 60 mm Hg (Echo)
PAP, mean	TRV > 3.4 m/s or > 2.8 m/s + signs of PH (Echo)
PAPM	TRV ≥ 2.8 m/s (Echo)
PAPm	TRV graded according to European Society of Cardiology Guidelines (Echo)
PAPs	mPAP ≥ 20 mm Hg (RHC)
PAPsys	mPAP > 20 mm Hg (RHC)
PAPsyst	mPAP ≥ 21 mm Hg (RHC)
PASP	mPAP > 21 mmHg and pulmonary vascular resistance ≥ 3 wood units (RHC)
Peak TR systolic gradient + central venous pressure	mPAP ≥ 25 mmHg (RHC) or TRV ≥ 3.5 m/s (Echo)
Peak TR velocity	mPAP ≥ 25 mmHg (RHC) or sPAP > 40 mmHg (Echo)
Peak tricuspid regurgitation jet	mPAP ≥ 25 mmHg and pulmonary vascular resistance/systemic vascular resistance > 0.3 (RHC)
Peak tricuspid regurgitation systolic gradient + central venous pressure	mPAP ≥ 25 mmHg (RHC)
Peak tricuspid regurgitation velocity	mPAP ≥ 25.5 mmHg (RHC)
Pressure gradient tricuspid regurgitation	mPAP > 25 mmHg at rest or > 30 mmHg exercise (RHC)
PSAP (pulmonary systolic arterial pressure)	mPAP > 25 mmHg (RHC)
Pulmonary arterial systolic pressure	mPAP > 25 mmHg and pulmonary arterial wedge pressure ≤ 15 mmHg (RHC)
Pulmonary artery systolic pressure	mPAP > 25 mmHg (RHC) or sPAP > 40 mmHg (Echo)
Pulmonary pressure	mPAP > 30 mmHg (RHC)
Right ventricular gradient	mPAP > 35 mmHg (RHC)
RV/RA-gradient	Defined by ICD or Billing Codes
RVESP (right ventricular estimated systolic pressure)	PH definition not specified
RVPG (right ventricular pressure gradient)	PH defined as Pulmonary Arterial Hypertension (PAH)
RVSP	
Systolic artery pressure	
Systolic PAP	

(Continues)

TABLE 1 | (Continued)

PAP Nomenclature in ECHO and RHC	PH definitions in the literature
Systolic Pulmonary Atrial Pressure	
Systolic RV pressure	
Systolic TR velocity	
TR	
TR velocity	
Transtricuspidal pressure gradient	
Tricuspid regurgitation jet velocity	
TRPG (tricuspid regurgitation pressure gradient)	
TRVmax (maximal tricuspid regurgitation velocity)	

In the right column, for the sake of clarity, "sPAP," "mPAP," and "TRV" were used instead of the original terms for "PAP".
PAP = pulmonary arterial pressure; sPAP = systolic PAP; mPAP = mean PAP; PH = pulmonary hypertension; TRV = tricuspid regurgitation velocity; RV = right ventricle; RAP = right atrial pressure; RA = right atrium; TR = tricuspid regurgitation.

consensus statements should be reported, as well as quantitative data for TRV/PAP. In addition, the rationale for selecting thresholds that are alternative to the standard definition should be provided to avoid confusion. When reporting PH, accurate descriptions of population age and sex distribution, PH-associated co-morbidities, social determinants of disease, as well as geographic region may also help optimize description of cohorts to improve alignment between the PH framework used in clinical practice and empiric research. In conclusion, approximating nomenclature used in empiric research with the clinically relevant PH definition is needed to avoid confusion and unnecessary variability in data characterizing this important and highly morbid disease.

Author Contributions

Armella Santi, Katarina Zeder, and Bradley A. Maron contributed to writing, contextualizing, and editing. Veranyuy Ngah and Eric W. Robbins edited and provided final approval. All authors approved the final manuscript. Katarina Zeder and Bradley A. Maron are the guarantors.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

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References

1. S. Hatano and T. Strasser, World Health Organization, Primary Pulmonary Hypertension: Report on a WHO Meeting, Geneva, 15–17 October 1973, 1975.

2. M. Humbert, G. Kovacs, M. M. Hoeper, et al., "2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension," *European Respiratory Journal* 61, no. 1 (2023): 2200879, Print 2023, https://doi.org/10.1183/13993003.00879-2022.

3. M. R. Fisher, P. R. Forfia, E. Chamera, et al., "Accuracy of Doppler Echocardiography in the Hemodynamic Assessment of Pulmonary Hypertension," *American Journal of Respiratory and Critical Care Medicine* 179, no. 7 (2009): 615–621.

4. G. Kovacs, S. Bartolome, C. P. Denton, et al., "Definition, Classification and Diagnosis of Pulmonary Hypertension," *European Respiratory Journal* 64, no. 4 (2024): 2401324, Print 2024, https://doi.org/10.1183/13993003.01324-2024.

5. N. Galie, M. Humbert, J. Vachiery, et al, "2015 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by Association for European Paediatric and Congenital Carogy (AEPC), International Society for Heart and Lung Transplantation (ISHLT)," *European Heart Journal* 37, no. 1 (2016): 67–119.

6. M. Lindstrom, N. DeCleene, H. Dorsey, et al., "Global Burden of Cardiovascular Diseases and Risks Collaboration, 1990–2021," *Journal of the American College of Cardiology* 80, no. 25 (2022): 2372–2425.

7. T. Vos, S. S. Lim, C. Abbafati, et al., GBD 2019 Diseases and Injuries Collaborators, "Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019," *Lancet* 396, no. 10258 (2020): 1204–1222.

8. J. H. Huston, B. A. Maron, J. French, et al., "Association of Mild Echocardiographic Pulmonary Hypertension With Mortality and Right Ventricular Function," *JAMA Cardiology* 4, no. 11 (2019): 1112–1121.

9. B. A. Maron, E. Hess, T. M. Maddox, et al., "Association of Borderline Pulmonary Hypertension With Mortality and Hospitalization in a Large Patient Cohort: Insights From the Veterans Affairs Clinical Assessment, Reporting, and Tracking Program," *Circulation* 133, no. 13 (2016): 1240–1248.